REMARKS

Claims 1, 2, 19-27 are currently pending in the instant application. Claims 28-32 are added. Thus, upon entry of the above amendments, Claims 1, 2, and 19 to 32 will be pending. The new claims are fully supported by the present specification. For example, claims 28 and 31 are supported at Example 13 at pages 58 to 65, and Table 1 at page 63; claim 29 and 32 are supported at page 2, lines 9 to 11, Example 13 at pages 58 to 65, and Table 2 at page 64. Claim 30 is supported at page 3, line 24 to page 4, line 22. No new matter is introduced by the new claims.

Claims 1, 2, 19-27 are drawn to a method for inhibiting the growth of cancer cells in a patient, wherein the method comprises administering to the patient an antagonist of the DNA binding activity of STAT. New claims 28-32 are drawn to a method for inhibiting the growth of cancer cells in a patient, wherein the method comprises administering to the patient an inhibitor of STAT dimerization or an antagonist of SH2-pY interaction.

In the instant Communication, the Examiner has withdrawn claims 26 and 27 from further consideration, as being drawn to a non-elected invention, because the limitations recited in claims 26 and 27 appear applicable to claims drawn to methods comprising administering an inhibitor of STAT dimerization or an antagonist of an SH2-pY interaction, respectively. However, the Examiner states that if Applicants were to provide factual evidence indicating that the peptides of claims 26 and 27 are capable of inhibiting STAT DNA binding, rejoinder of the claims will be proper. Further, the Examiner points out that if the peptides of claims 26 and 27 are also able to inhibit STAT dimerization and/or SH2-pY interaction, the restriction requirement set forth in the Office Action mailed July 2, 2002 (Paper No. 13) would have to be reconsidered, since in such a case, groups I, V, and VII might have to be rejoined.

Applicants appreciate the Examiner's invitation to provide factual evidence showing that the peptides of claims 26 and 27 are capable of inhibiting DNA STAT binding and his willingness to reconsider rejoinder of groups I, V, and VII. Indeed, as taught in the instant specification, Applicants explain hereinbelow that a peptide that inhibits SH2-pY interaction also inhibits STAT dimerization, and thereby inhibits STAT DNA binding activity.

In particular, Applicants direct the Examiner's attention to the instant specification at page 2, lines 7 to 11, and 21 to 24, and page 4, lines 8 to 9, where is described

the relationship among SH2-pY interaction, STAT dimerization, and STAT DNA binding activity. As pointed out in the specification, monomeric, inactive STAT proteins associate with each other to form active dimers through a key phosphotyrosine (pY) residue, which binds to the SH2 domain of another STAT monomer. Depending on which STAT family members are activated, STATs may associate as homodimers or heterodimers, and then translocate to the nucleus, whereupon the activated STAT dimers bind to specific DNA-response elements in promoters, and induce expression of target genes. Thus, SH2-pY interaction is required for STAT dimerization, and STAT dimerization is required for STAT DNA binding activity. As such, a peptide that disrupts SH2-pY interaction will disrupt STAT dimerization and thereby disrupt STAT DNA binding activity. A peptide that disrupts STAT dimerization will also disrupt STAT DNA binding activity.

Example 13 at pages 58 to 65 of the present application describes small peptides that bind to full-length STAT3, bind the SH2 domain of STAT3, and/or disrupt STAT3 DNA-binding activity. High-throughput screening methods are used to obtain such small peptides. The high-throughput screening methods are designed partially based on the relationship among SH2-pY interaction, STAT dimerization, and STAT DNA binding activity. For example, an assay specifically designed to detect disruption of phosphotyrosine-SH2 interaction is based on a synthetic peptide corresponding to the tyrosine phosphorylation site in STAT3 and surrounding sequence, which mediates STAT3 homodimer formation. See specification, page 62, line 24 to page 63, line 12. In a high throughput screening assay used to measure STAT3 DNA-binding activity, the assay is designed to provide activated STAT3 dimers by using a baculovirus expression system expressing STAT3 and a tyrosine kinase. See specification, page 61, line 20 to page 62, line 11. Because of the way the high-throughput screening methods were designed and the relationship among SH2-pY interaction, STAT dimerization, and STAT DNA binding activity described in the specification, it would be understood by a person skilled in the art that a peptide that inhibits SH2-pY interaction and/or STAT dimerization, will also inhibit STAT DNA binding activity.

Furthermore, Applicants submit that Turkson *et al.*, 2001, J. of Biol. Chem. 48:45443-45455 (reference CB, hereinafter "Turkson") presents experimental evidence suggesting that a phosphopeptide that binds to the STAT3 SH2 domain and reduces STAT3 DNA binding activity also disrupts STAT3 dimerization.

Turkson used the phosphopeptide PY*LKTK (Y* represents phosphotyrosine) (which is the same as the first peptide described in Table 3, page 64 of the present application), and its tripeptide derivative sequences, PY*L and AY*L (which are the same as the last two peptides described in Table 3, page 65 of the present application, respectively), which were derived from the sequence of amino acids in the vicinity of pY in the SH2-binding region of STAT3. The prediction by the authors of Turkson was that PY*LKTK peptide will bind to STAT3, preventing the SH2-pY interaction between two monomeric STAT3 molecules, and disrupting dimerization and DNA binding activity, which can be measured by an electrophorectic mobility shift assay (EMSA).

Turkson presented experiments suggesting that PY*LKTK engaged in direct pY-SH2 interactions with STAT3 and disrupted the formation of STAT3:STAT3 dimers. See Turkson, page 45448, column 1, line 4 from the bottom, to page 45449, the end of the first full paragraph. Furthermore, EMSA confirmed that the presence of PY*LKTK resulted in a dose-dependent decrease in the level of STAT3 binding to an oligonucleotide probe. See Turkson, page 45445, column 1, line 19 from the bottom, to column 2, line 9.

Accordingly, in view of the foregoing, there is evidence that a peptide that disrupts SH2-pY interactions and/or inhibits STAT dimerization also interferes with STAT DNA binding activity.

In view of the foregoing, rejoinder of claims 26 and 27 is proper. Further, as the Examiner suggested, the restriction requirement set forth in the Office Action mailed July 2, 2002 (Paper No. 13) should be reconsidered, and groups I, V, and VII of that Office Action should be rejoined.

Restriction Requirement under 35 U.S.C. § 121

The Examiner has further required an election under 35 U.S.C. § 121 of one of following inventions:

I. Claims 1, 2, 19 and 20, insofar as the claims are drawn to a method for inhibiting the growth of cancer cells in a patient, wherein said method comprises administering to said patient an antagonist of the DNA binding activity of STAT, wherein said antagonist is an antibody, classified in class 424, subclass 138.1.

II. Claims 1, 2, 19, and 21-25, insofar as the claims are drawn to a method for inhibiting the growth of cancer cells in a patient, wherein said method comprises

administering to said patient an antagonist of the DNA binding activity of STAT, wherein said antagonist is a peptide comprising one of the amino acid sequences selected from the group of amino acid sequences consisting of those recited in claim 25, classified in class 514, subclasses 12-18.

The Examiner contends that Groups I and II are distinct, each from the other.

In order to be fully responsive, Applicants hereby provisionally elect the invention of Group II, claims 1, 2, 19, and 21-25, drawn to a peptide comprising one of the amino acid sequences selected from the group of amino acid sequences consisting of those recited in claim 25, classified in class 514, subclasses 12-18, with traversal. For reasons stated above, Applicants believe that claims 26, 27 and new claims 28-32 are also within the elected group.

With respect to the Examiner's division of the invention into two groups and the reasons stated therefor, Applicants respectfully traverse.

Even assuming *arguendo* that Groups I and II represented distinct or independent inventions, Applicants submit that to search the subject matter of the two Groups together would not be a serious burden on the Examiner. The M.P.E.P. § 803 (Eighth Edition, August 2001, revised February 2003) states:

> If the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions.

Thus, in view of M.P.E.P. §803, all of the subject matter of Groups I and II should be searched and examined together.

Accordingly, Applicants respectfully request that the Restriction Requirement under 35 U.S.C. §121 be withdrawn and the instant claims be examined in one application.

Applicants retain the right to petition from the restriction requirement under 37 C.F.R. §1.144.

CONCLUSION

Applicants respectfully request that the present amendments and remarks be made of record in the instant application. An allowance of the application is earnestly requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted,

Date: June 30, 2003

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